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THE INTERACTION OF METHYLENE CHLORIDE AND THE SODIUM DERIVATIVE OF ETHYL MALONATE

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CIX.—*The Interaction of Methylene Chloride and the Sodium Derivative of Ethyl Malonate.*

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Perkin and Prentice (Trans., 1891, 59, 991) have described a synthesis of ethyl propanetetracarboxylate by the condensation of methylene chloride with the sodium derivative of ethyl malonate, and, as a by-product of the reaction, obtained a quantity of a yellow, crystalline substance which contained sodium.

Having had occasion to prepare ethyl propanetetracarboxylate, I employed the method described by Perkin and Prentice, and a quantity of the above-mentioned yellow by-product was isolated. After communicating with Prof. Perkin on the subject, this product was submitted to as complete an examination as was possible with

the relatively small amount of material available. Two other crystalline by-products of the reaction were also investigated.

It has been found that the substances produced by the condensation of methylene chloride with the sodium derivative of ethyl malonate vary according to the conditions under which the reaction takes place. Six experiments were conducted, in three of which the mode of procedure was as follows. Ethyl malonate (64 grams) was added to a cold alcoholic solution of sodium ethoxide (9·2 grams Na in 200 c.c. of alcohol), after which the liquid became thick, owing to the separation of the sodium derivative of the ester. Methylene chloride (17 grams) was then added, thoroughly mixed, and the turbid liquid placed in four soda-water bottles and heated at 100° for two hours. At the end of this time the contents of the bottles no longer gave an alkaline reaction, but had a bright yellow colour and contained a quantity of a bulky solid. The alcohol was then removed by distillation, and, on fractionation, was found to contain about half the methylene chloride originally employed. Sufficient water was added to the pasty residue to dissolve the solid which it contained, and the esters were extracted from the resulting mixture by means of ether. During this operation a large quantity of the yellow sodium salt, observed by Perkin and Prentice, separated and was collected. The ethereal solution was washed with water until the aqueous liquid was no longer bright yellow, dried, and the ether removed. On fractionating the residual oil under 80 mm. pressure it was found that rather more than half of it consisted of unchanged ethyl malonate, the remainder being crude ethyl propanetetracarboxylate. The yield of the propane compound was never more than 20 per cent. of that theoretically possible, whereas that recorded by Perkin and Prentice was about 60 per cent. It may also be noted that on careful fractionation the boiling point of the ethyl propanetetracarboxylate was found to be 244°/80 mm., and not 234—236°/80 mm. as recorded by the previous investigators.

The aqueous liquid from which the esters had been separated by means of ether was acidified with sulphuric acid, when a quantity of a heavy oil was precipitated. After extracting this with ether, and completely removing the solvent, it slowly deposited a small amount of a crystalline *substance* which was removed by filtration. This substance dissolved readily in hot ethyl acetate, from which it separated in needles melting at 132°. On examining the oil which had been freed from the crystalline substance, it was found to contain some malonic acid, together with a small amount of the acid which yields the above-mentioned yellow sodium salt, but no other substance could be isolated from it.

Three other condensations were carried out in the manner already described, with the exception that the sodium was dissolved in only 150 c.c. of the alcohol, the other 50 c.c. being employed to dilute the malonic ester before mixing it with the sodium ethoxide. Working in this manner it was found that the sodium derivative of the ethyl malonate never separated, the liquid remaining quite clear. On heating this solution for two hours with methylene chloride it did not become so yellow, nor did it deposit so much solid as was the case in the experiments previously described, and it yielded none of the yellow sodium salt.* This was, moreover, not the only difference, for, although there was about the same yield of ethyl propanetetracarboxylate, considerably more unchanged ethyl malonate was recovered. Furthermore, the examination of the aqueous liquid from which the esters were separated yielded a different result. The heavy oil which was precipitated on acidifying the solution was extracted as in the previous experiments, but on standing, in addition to the compound melting at 132°, it deposited a *substance* which was insoluble in ethyl acetate.

As both unchanged ethyl malonate and methylene chloride were among the substances isolated from the reaction mixture, it appeared probable that the yield of ethyl propanetetracarboxylate might be increased if, at the end of two hours' heating, a further quantity of sodium ethoxide were added to the contents of the soda-water bottles, and the mixture again heated; this was found to be the case.

By employing methylene iodide in place of the chloride, and heating the mixture on a water-bath in a flask attached to a reflux condenser, Guthzeit and Dressel (*Annalen*, 1890, **256**, 171) obtained a yield of ethyl propanetetracarboxylate amounting to 84 per cent. of that theoretically possible. An experiment was therefore conducted with the use of methylene iodide, but the mixture was heated in soda-water bottles at 100°. Under these conditions it was found that the product consisted entirely of about equal proportions of ethyl malonate and ethyl methylenemalonate, no ethyl propanetetracarboxylate being obtained.

Examination of the Yellow Sodium Salt.

The yellow sodium salt, which was obtained in glistening leaflets, was purified by recrystallisation from alcohol:

0·1288 gave 0·0191 Na_2CO_3. Na = 6·4.

$C_{14}H_{21}O_6 \cdot CO_2Na$ requires Na = 6·5 per cent.

* In one experiment, where the heating had been prolonged to three hours, very small amount of this salt was obtained.

On treatment with sulphuric acid this salt yielded a liquid *acid* which gave a deep violet coloration with ferric chloride:

0·1314 gave 0·2630 CO_2 and 0·0798 H_2O. C = 54·6; H = 6·7.
0·1304 „ 0·2607 CO_2 „ 0·0786 H_2O. C = 54·5; H = 6·7.
$C_{15}H_{22}O_8$ requires C = 54·5; H = 6·6 per cent.

0·2148 neutralised 6·7 c.c. *N*/10 NaOH.
$C_{14}H_{21}O_6 \cdot CO_2H$ requires 6·5 c.c.

A molecular weight determination by the cryoscopic method gave the following result:

0·3160 dissolved in 33 of phenol gave Δ^t - 0·220°. M.W. = 331.
$C_{15}H_{22}O_8$ requires M.W. = 330.

From these results it appears that the yellow by-product is the sodium salt of an acid possessing the formula $C_{14}H_{21}O_6 \cdot CO_2H$.

Hydrolysis of the Acid $C_{14}H_{21}O_6 \cdot CO_2H$.—A quantity of the yellow sodium salt was boiled with a large excess of an aqueous solution of potassium hydroxide. During the first half-hour the yellow colour of the liquid became deeper, and it was found that if the hydrolysis was stopped at the end of this time, the liquid acidified and extracted with ether, an *acid* melting at 305° was obtained. When, however, the heating was continued for five hours, the solution became colourless, and, on acidifying and extracting with ether, it then yielded an *acid* which, when crystallised from ethyl acetate, melted at 138—139°:

0·1053 gave 0·1782 CO_2 and 0·0447 H_2O. C = 46·1; H = 4·7.
0·0987 „ 0·1662 CO_2 „ 0·0418 H_2O. C = 45·9; H = 4·7.
$C_{10}H_{12}O_8$ requires C = 46·1; H = 4·6 per cent.

0·1172 neutralised 18·3 c.c. *N*/10 NaOH.
$C_6H_8(CO_2H)_4$ requires 18·1 c.c.

The acid melting at 138—139°, therefore, possesses the formula $C_6H_8(CO_2H)_4$. It is a saturated compound, and must therefore contain in its structure a closed ring. Although it melts at the same temperature as *cis-cyclo*hexane-1 : 2 : 4 : 5-tetracarboxylic acid (Gregory and Perkin, Trans., 1903, **83**, 787), the two compounds are not identical, as the *barium* and *calcium* salts of the acid here described are readily soluble in water, the latter salt crystallising in needles from dilute alcohol. Moreover, the acid obtained by the hydrolysis of the yellow sodium salt does not yield a dianilic acid similar to that prepared from the *cyclo*hexane acid, but gives a *compound* (m. p. 224°) which is insoluble in aqueous alkalis.

The formation of a tetracarboxylic acid, $C_{10}H_{12}O_8$, by the hydrolysis of a monocarboxylic acid possessing the formula $C_{15}H_{22}O_8$, would seem to indicate that the latter compound was the diethyl mono-methyl ester of the former, but it is difficult to see how this can

be the case. Moreover, a compound that was simply a tri-ester of a tetracarboxylic acid would not be expected to yield a coloured sodium salt or to give a violet coloration with ferric chloride. These considerations, together with the fact that the tetracarboxylic acid is not the first product of the hydrolysis of the yellow sodium salt, but is only produced by prolonged action of the alkali, lead to the conclusion that the acid, $C_6H_8(CO_2H)_4$, is not formed by simple hydrolysis of the acid $C_{14}H_{21}O_6{\cdot}CO_2H$, but is the product of some more profound change.

Examination of the Substance Melting at 132°.

The substance melting at 132°, obtained as previously described, crystallises from a mixture of alcohol and ethyl acetate in flattened needles. It is very slightly volatile in steam, and gives a deep wine-red colour with ferric chloride:

0·0985 gave 0·2034 CO_2 and 0·0557 H_2O. C = 56·3 ; H = 6·3.
0·1004 „ 0·2074 CO_2 „ 0·0576 H_2O. C = 56·3 ; H = 6·3.
$C_{20}H_{26}O_{10}$ requires C = 56·3 ; H = 6·1 per cent.
0·1000 neutralised 4·3 c.c. *N*/10 NaOH.
$C_{18}H_{24}O_6(CO_2H)_2$ requires 4·6 c.c.

When hydrolysed with potassium hydroxide, this compound gave an *acid* which crystallised from alcohol in plates melting at 306°, gas being suddenly evolved.

Examination of the Substance Insoluble in Ethyl Acetate.

This product consisted of minute, slightly yellow needles, which were insoluble, or nearly so, in all solvents. When heated it assumed a deep orange colour, and decomposed above 295°. It was heated with a dilute solution of sodium carbonate, when it was gradually hydrolysed and dissolved. On cooling the solution, a *sodium* salt separated in white needles:

0·1600 of salt crystallised from water, on heating at 125°, lost 0·0182 H_2O. H_2O = 11·4.
0·1418 of anhydrous salt gave 0·0369 Na_2SO_4. Na = 8·4.
0·0905 „ „ 0·0175 Na_2CO_3. Na = 8·4.
$C_{32}H_{35}O_{20}Na_3,6H_2O$ requires H_2O = 11·7 per cent.
$C_{32}H_{35}O_{20}Na_3$ requires Na = 8·5 per cent.

The corresponding *potassium* salt is insoluble in water and is anhydrous; it can be crystallised from glacial acetic acid:

0·1049 gave 0·0325 K_2SO_4. K = 13·8.
$C_{32}H_{35}O_{20}K_3$ requires K = 13·7 per cent.

The acid was prepared in the following manner. The salt was

dissolved in warm concentrated hydrochloric acid, water then immediately added, and the precipitated *acid* collected on a filter. These operations must be conducted as rapidly as possible, as the organic acid is readily acted on by the mineral acid. The acid prepared in this way crystallises from ethyl acetate in leaflets melting at 200°, and gives an intense reddish-brown coloration with ferric chloride:

0·1117 gave 0·2132 CO_2 and 0·0526 H_2O. C = 51·8; H = 5·2.
0·1096 ,, 0·2084 CO_2 ,, 0·0527 H_2O. C = 51·8; H = 5·3.
$C_{32}H_{38}O_{20}$ requires C = 51·8; H = 5·1 per cent.

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